BRACHIAL PLEXUS BLOCK WITH BUPIVACAINE: EFFECTS OF ADDED ALPHA-ADRENERGIC AGONISTS: COMPARISON BETWEEN CLONIDINE AND EPINEPHRINE

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CERTIFICATE

This is to certify that the dissertation entitled, " BRACHIAL PLEXUS BLOCK WITH BUPIVACAINE: EFFECTS OF ADDED ALPHA-ADRENERGIC AGONISTS: COMPARISON BETWEEN CLONIDINE AND EPINEPHRINE" SUBMITTED BY Dr.V.S.SURESH in partial fulfillment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamilnadu Dr.M.G.R. Medical University, Chennai is a bonafide record of the work done by him in the Department of Anaesthesiology, Madras Medical College, during the academic year 2006 -2009.

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CONTENTS

INTRODUCTION

Peripheral nerve blocks provide ideal operating conditions when used optimally. They are said to cause least interference with the vital physiological functions of the body and reduced stress response avoiding polypharmacy with an alert, awake and co-operative patient when compared to other conventional techniques. Adequately administered regional anaesthesia can not only provide excellent intraoperative pain relief but also good post operative analgesia.

Regional anaesthesia traces its origin to Dr.Carl Koller, a young Viennese Opthalmologist, who in 1884 employed a solution of cocaine for topical corneal anaesthesia in patients undergoing eye surgeries. Most of the local anaesthetic agents developed in the first half of 20th century (1900 – 1940) were basically amino ester compounds. They lost their importance due to their shorter duration of action and associated allergic reactions and systemic toxicity. This paved the way for the synthesis of newer agents namely the aminoamide compounds. The advent of long acting drugs have made it possible to carry out prolonged surgeries in the extremities especially for Vascular ,Orthopaedic and Plastic procedures and also for relief of chronic pain. The main drawbacks of these agents were the delayed onset of action, varying quality of blockade and inadequate post operative analgesia. To overcome these problems various additives were tried along with local anaesthetic solutions.

Brachial Plexus block[1] was first performed by William Stewart Halsted in 1889. He directly exposed the brachial plexus in the neck to perform the block and used cocaine. Hirschel first described the percutaneous approach to the brachial plexus. Kulenkampff first described the classical supraclavicular approach to the brachial plexus. The

subclavian perivascular block was first described by Winnie and Collins. The infraclavicular approach was first developed by Raj. The axillary approach was first performed by Accardo and Adriano in 1949.

The demonstration of α-adrenorecepors in the Peripheral nervous system prompted many investigations on the effects of using various α-adrenergic drugs in combination with local anaesthetics for peripheral nerve blocks to prolong post operative analgesia.

The present study is designed to compare the efficacy of added alpha adrenergic agonist clonidine and epinephrine for prolongation of post operative analgesia when added to bupivacaine in the Brachial Plexus block.

AIM OF THE STUDY

The aim of the study is:

a. To compare the effects of alpha adrenergic agonists Clonidine and adrenaline as an adjuvant to bupivacaine in blocking brachial plexus by supraclavicular approach in patients undergoing upper limb surgeries.

The following parameters are compared

* Onset of sensory and motor blockade

* Duration of sensory blockade

* Haemodynamic stablity

b. To study the associated complications of the procedure.

APPLIED PHYSIOLOGY

PHYSIOLOGY OF NERVE CONDUCTION: [2]

Neurons are the basic building blocks of the nervous system that respond to various stimuli. Integration and transmission of nerve impulses are specialised functions of neurons.

All peripheral nerves are elongated axons of neurons situated centrally. A typical peripheral nerve consists of bundles of motor, sensory and other fibres enclosed in the outermost covering called epineurium. Inside the epineurium, the perineurium surrounds the collection of bundles. Each bundle is surrounded by an endoneurium. Each nerve fibre in a bundle is enclosed in a layer of neurilemma or the axonal membrane.

Depending on the presence or absence of myelin sheath, it can be a myelinated nerve fibre or unmyelinated nerve fibre.

The axonal membrane itself is made up of a bimolecular lipid palisade, interspersed with large protein molecules. The membrane lipids are largely phospholipids composed of a polar head group and a non polar hydrocarbon tail.

The primary function of the cell membrane is to separate the extracellular from the intracellular environment. The major difference between these two environments is the ionic concentration. This disequilibrium provides the means for impulse conduction.

The most important ions in this respect are Sodium and Potassium. A membrane bound protein sodium potassium ATPase maintains normal

resting equilibrium potential between -50mv to -90mv by pumping sodium ions out

of the cell and potassium ions into the cell. A positive ion gradient from inside the membrane to the outside causes electro negativity inside the membrane.

During nerve conduction the following changes occur in the cell membrane.

IN THE RESTING PHASE:

There is a potential difference across the membrane inside is negative, due to a higher concentration of Sodium ions outside than inside the cell.

K^+ moves out of cells and Na^+ moves in but because of more K^+ channels opened at rest, K^+ permeability is greater than Na^+ permeability. Therefore K^+ channels maintain the resting membrane potential.

DEPOLARIZATION PHASE:

During excitation, Na^+ channels in the cell membrane open briefly allowing sodium ions to flow into the cell, thereby depolarizing the membrane.

REPOLARIZATION PHASE:

During this phase, opening of voltage gated K^+ channel occurs, results in passing of Potassium ions out of the cell to restore electrical neutrality.

RESTORATION PHASE:

During this phase, sodium ions return to the outside and potassium ions re-enter the cell.

DISTRIBUTION OF ION CHANNELS IN MYELINATED NEURONS:

Voltage gated Na^+ channels are highly concentrated in the nodes of Ranvier and the initial segment in myelinated neurons.

The initial segment and in sensory neurons, the first node of Ranvier are the sites where impulses are normally generated and the other nodes of Ranvier are the sites to which the impulses jump during saltatory conduction.

The sodium channel is believed to be an integral membrane spanning protein. The three dimensional configuration of the proteins forms a pore through the neuronal membrane.

Depolarization of the cell induces a configurational change on the sodium channel which causes it to open and allow ion passage.

In many myelinated neurons, the Na^+ channels are flanked by K^+ channels that are involved in repolarization.

ACTION OF LOCAL ANAESTHETICS ON NERVE FIBRES: [3]

The primary action of local anaesthetics on the nerves is electrical stabilization. The large transient increase in permeability to Na^+ ions necessary for propagation of the nerve impulse is prevented. Thus the

resting membrane potential is maintained and depolarization in response to stimulation is inhibited.

Local anaesthetics block sodium conductance by:

1. Binding of local anaesthetics to sites on voltage gated Na^+ channels prevents opening of the channels by inhibiting the conformational changes that underlie channel activation.
2. Local anaesthetics produce nonspecific membrane expansion. There is an unfolding of membrane protein together with a disordering of the lipid component of the cell membrane with consequent obstruction of the sodium channel.

Action of alpha adrenergic agonists on nerve fibres produces antinociception in a variety of ways.

a. The α-2 adrenoreceptors are located on the afferent terminals of both peripheral neurons and neurons in the superficial laminae of the spinal cord, and within several brainstem nuclei implicated in analgesia.
b. Clonidine partially inhibits voltage gated Na^+ and K^+ channels and suppresses the generation of action potentials in tonic firing neurons.
c. Some contribution by the release of acetylcholine in the neuraxial region.
d. Some degree of blockade by blocking the C-fibres in the peripheral nerves.

ANATOMY OF THE BRACHIAL PLEXUS

THE BRACHIAL PLEXUS: [6] FIG - 1

Brachial Plexus is one of the most commonly used peripheral nerve blocks in clinical practice. So knowledge of the formation of the brachial plexus and of its distribution is absolutely essential for the effective use of brachial plexus block for surgeries of the upper limb. Absolute familiarity with the Vascular, Muscular and fascial relationship of the brachial plexus throughout its formation and distribution is equally essential for the mastery of various techniques of brachial plexus anaesthesia.

In its course from the intervertebral foramina to the upper arm, the fibres that constitute the plexus are composed consecutively of roots, trunks, cords, divisions and terminal nerves which are formed through a complex process of combining, dividing, recombining and finally redividing.

FORMATION OF THE PLEXUS:

ROOTS:

The plexus is formed by the anterior primary rami of 5th to 8th cervical plexus together with the bulk of the 1st thoracic nerve (C_8-T_1). In addition, there is frequently a combination from C_4 to the 5th cervical roots and another below the T_2 to the 1st thoracic nerve. Occasionally the plexus is mainly derived from C_4-C_8 (prefixed plexus) or from C_6-T_2 (post fixed plexus).

TRUNKS:

The five roots of the brachial plexus emerge from the intervertebral foramina. They lie in the gutter between the anterior and posterior tubercles of the corresponding transverse process. All five roots then become sandwiched between Scalenus anterior and Scalenus medius. Here the roots of C_5 and C_6 unite into the upper trunk, the root of C_7 continues as the middle trunk and those of C_8 and T_1 into the lower trunk. Each trunk divides behind the clavicle, into anterior and posterior divisions which unite in the axilla to form cords.

CORDS:

The six divisions stream into axilla and there join up into three cords; lateral, medial and posterior. These cords are composed as follows:

The union of the anterior divisions of the Upper and middle trunks form the lateral cord. The medial cord represents the continuation of the anterior division of the lower trunk. The posterior cord comprises of the posterior divisions of all the three trunks. The composition of brachial plexus can be summarised as follows:

1. Five roots (between the scalene muscles) - the anterior primary rami of C_5-C_8 and T_1.

2. Three trunks (in the posterior triangle)

    a) Upper trunk C_5 and C_6

    b) Middle trunk C_7 alone

FIG - 3

c) Lower trunk C_8 and T_1

3. Six divisions (behind the Clavicle)

   Each trunk divides into an anterior and posterior division.

4. Three cords (within the axilla)

   a) Lateral Cord - the fused anterior divisions of the upper and middle trunks C_5 - C_7

   b) Medial Cord - the anterior division of the lower trunk C_8 - T_1

   c) Posterior Cord formed by the union of the posterior divisions of all three trunks C_5-T_1

RELATIONS OF THE BRACHIAL PLEXUS: FIG – 2 & 3

ROOTS:

Lie between the Scalenus anterior and Scalenus medius. The roots of the Plexus lie above the second part of the subclavian artery.

TRUNKS:

In the Posterior triangle, the trunks of the plexus invested in a sheath of prevertebral fascia, are superficially placed, being covered by skin, platysma and deep fascia.

The upper and middle trunks lie above the subclavian artery as they stream across the first rib, but the lower trunk like behind the artery and may groove the rib immediately posterior to the subclavian groove.

DIVISIONS:

At the lateral border of the first rib, the trunks bifurcate into divisions which are situated behind the clavicle, subclavius muscle and the suprascapular vessels.

CORDS:

The cords are formed at the apex of the axilla and become grouped around the axillary artery.

THE INTERSCALENE SHEATH:

As the roots emerge in the groove between the transverse process of the tubercle, they lie in a fibrofatty space between two layers of fibrinous sheath. Posterior Sheath from the posterior tubercles covers the front of the medius, anterior sheath from anterior tubercles cover the posterior aspect of the Scalenus anterior. The sheath extends into the axilla around the plexus. Significance of this space is that the local anaesthetic can be injected to produce block at various sites by interscalene, subclavian perivascular or the axillary approach.

SYMPATHETIC SUPPLY:

Close to the emergence the 5th and 6th Cervical nerves receive a grey ramus from the middle cervical sympathetic ganglion. The 7th and 8th cervical nerves each receive a

grey ramus from the inferior cervical ganglion and from T1ganglion

BRANCHES:

Branches are given off from roots, trunks and cords.

1. Branches from the roots:

   a) Nerve to the serratus anterior C_5, C_6 and C_7

   b) Muscular branches to
      - Longus cervices C_5 - C_8
      - Three Scalene C_5 - C_8
      - Rhomboids C_5

   c) Twig to the Phrenic nerve C_5

2. Branches from the trunks:

   a) Suprascapular nerve C_5-C_6

   b) Nerve to subclavius C_5-C_6

3. Branches from the Cords:

a) Lateral Cord

- Lateral Pectoral nerve C_5-C_7
- Lateral head of median nerve C_5-C_7
- Musculocutaneous nerve C_5-C_7

b) Medial Cord

- Medial Pectoral nerve C_8 - T_1
- Medial head of median nerve C_8 - T_1
- Medial Cutaneous nerve of arm C_8 - T_1
- Medial Cutaneous nerve of forearm C8 - T1
- Ulnar nerve of arm C7, C8 - T1

c) Posterior Cord

- Upper Subscapular nerve C_5-C_6
- Lowe Subscapular nerve C_5-C_6
- Nerve to latissimus dorsi C_6, C_7, C_8
- Axillary nerve C_5-C_6

- Radial nerve C_5, C_6, C_7, C_8, T_1

ANATOMIC CONSIDERATIONS OF THE INTERSCALENE SPACE:

The roots of the brachial plexus, after leaving the transverse process of the corresponding cervical vertebrae, descend in between the scalenus anterior and medius in the posterior triangle of the neck.

Scalenus anterior arises from the anterior tubercles of the transverse processes of C_3 - C_6 Vertebrae. It is inserted into the scalene tubercle on the inner border of the first rib. The muscle lies anterior to the plexus and at its

insertion lies anterior to the subclavian artery which separates the plexus from its insertion. Scalenus medius arises from the posterior tubercles of the six lowest cervical vertebrae and is inserted into the upper surface of the first rib behind the groove made by the brachial plexus and the subclavian artery. Thus the plexus lies in front of the muscle.

The first rib lies in an almost horizontal plane being inclined slightly downwards and forwards. It passes below the clavicle at about the junction of its inner and middle thirds. The upper surface of first rib has two transverse grooves - an anterior one for the subclavian vein and a posterior one for the subclavian artery and the lowest trunk of the brachial plexus. On the inner border between the grooves is the scalene tubercle.

Brachial line runs in a straight line from the transverse process of the C_6 vertebra to the axillary artery in the axilla. It runs inferolaterally at an angle of 45degree from the horizontal plane and slightly forwards at 15 degree.

Techniques of Brachial Plexus Block:[1, 7]

Surgical anaesthesia of the upper extremity and shoulder can be achieved following neural blockade of the brachial plexus at various sites. The various approaches that can be used for this blockade is as follows:

FIG - 4

i) Interscalene approach

ii) Supraclavicular approach

   a) Classic approach

   b) Plumb bob technique

   c) Supraclavicular Perivascular technique

iii) Axillary approach

iv) Infraclavicular approach

v) Posterior approach

INTERSCALENE BRACHIAL PLEXUS BLOCK

TECHNIQUE:

In this technique plexus is blocked at the level of the C_6 vertebra. By standing at the side of the patient and after locating the interscalene groove, an intradermal wheal is raised at the point of needle insertion which is at the level of the cricoid cartilage. A 22

gauge 3.5 cm short bevel needle is inserted “at right angles to the skin in all planes” i.e. dorsal to the horizontal

planes. The needle is advanced slowly until paraesthesia sought in the shoulder or a nerve stimulator is used to evoke contractions in the deltoid or biceps brachialis muscle. 20 -40 ml of local anaesthetic injected after repeated aspiration to detect inadvertent entry into vertebral artery or dural cuff.

COMPLICATIONS:

1. Subarachnoid injection
2. Epidural blockade
3. Intravascular Injection
4. Pneumothorax
5. Phrenic nerve block

SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK:

A. CLASSICAL SUPRACLAVICULAR BLOCK OF KULENKAMPFF:

In the classic approach, the needle insertion site is 1 cm superior to the clavicular midpoint. The needle is inserted in a plane parallel to the patient neck and head. The needle will contact the rib at a depth of 3 to 4 cm. The needle is walked over the rib until paraesthesia is elicited. After careful aspiration the local anaesthetic is injected.

B. PLUMB BOB SUPRACLAVICULAR BLOCK:

The brachial plexus at the level of the first rib lies posterior and cephalic to the subclavian artery. Once this skin mark has been placed

FIG – 5

immediately superior to the clavicle at the lateral border of the sternomastoid muscle as it is inserted into the clavicle, the needle is inserted at a 90 degree angle to the table top. The local anaesthesia is injected after eliciting paraestehsia. The name Plumb bob was chosen for this technique because if one suspends a Plumb bob over the entry site, needle inserted through that point will result in contact with the brachial plexus in most patients.

SUBCLAVIAN PERIVASCULAR TECHNIQUE OF WINNIE AND COLLINS: FIG - 5

The interscalene groove is palpated at its most inferior point, which is just posterior to the subclavian artery pulse. The needle is directed just above and posterior to the subclavian pulse and directed caudally at a flat angle against the skin. The needle is advanced until paraesthesia is elicited and the local anaesthetic is injected after careful aspiration.

COMPLICATIONS:

1. Pneumothorax
2. Horner's syndrome

3. Phrenic nerve block

4. Haemothorax and Haematoma formation.

INFRACLAVICULAR TECHNIQUE:

This is the preferred technique for the surgeries of elbow and lower arm because spread of local anaesthetic is kept below the clavicle. This technique blocks the brachial plexus at the level of cords. The needle is

inserted 1 inch beneath the midpoint of the clavicle. It is then directed laterally from this site at a 45 degree angle away from the chest wall and towards the humeral head or the coracoid process. Once paraethesia is elicited, the local anaesthetic is injected.

COMPLICATIONS:

1. Pneumothorax

2. Haemothorax

3. Chylothorax with a left side block

AXILLARY BRACHIAL PLEXUS BLOCK:

The pulsations of the axillary artery are best felt high in the axilla between the coracobrachialis and pectoralis major muscle. The needle is inserted just superior to the artery until the resistance of the fascial sheath is felt and a pop indicated the correct needle placement.

COMPLICATIONS:

1. Intra arterial Injection
2. Post Operative neuropathy
3. Hematoma and Infection.

STRUCTURE OF BUPIVACAINE

PHARMACOLOGY OF BUPIVACAINE: [8, 9, 10, 11]

Bupivacaine is an aminoacyl amide synthetic local anaesthetic synthesised by AF EKENSTAM et al at AB Botors (1957)[10]. Clinically used by Telivuion in 1963. It is produced for clinical use as a racemic mixture of the enantiomer containing equal proportions of the S and R forms.

PHYSIOCHEMICAL PROPERTIES:

Bupivacaine has a butyl group on the piperidine nitrogen atom of the molecule. It is a long acting local anaesthetic drug with high anaesthetic potency. It is more lipids soluble, highly protein bound and has greater intrinsic potency. It is 3 to 4 times as potent as lignocaine. It crosses the placenta and the blood brain barrier.

1.	Molecular weight base	288
2.	Pka	8.1
3.	Partition Coefficient	346
4.	Mean uptake ratio	3.3
5.	Protein binding	96%

PHARMACOLOGICAL PROPERTIES:

Onset	Moderate
Relative Potency	8
Duration of action	360 -720Min. [11]

MECHANISM OF ACTION:

Bupivacaine produces electrical stabilisation of the membrane by dual action on sodium conductance.

1. Acts directly on the receptors within the sodium channels.

2. Produces non specific membrane expansion.

PHARMACOLOGICAL EFFECTS:

a.	Local	Nerve blockade
b.	Regional	Pain, temperature, touch, motor power and vasomotor tone in the region supplied by the nerves are blocked
c.	Systemic	Effects occuring as a result of systemic absorption or intravenous administration.

On the cardiovascular system, the effect of bupivacaine is dose related. It depresses the automaticity of the heart and myocardial contractility. Depending on the membrane potential and the rate of stimulation, Bupivacaine depresses Vmax considerably more than lignocaine and results in slowed conduction of the cardiac action potential which is manifested as the prolongation of the PR and QR intervals on the electrocardiogram. This results in reentrant phenomenon and ventricular arrhythmias. The Na^+ channels are blocked in a fast - in slow-out manner which causes difficulty in resuscitation when the ventricular fibrillation has occured. The Cardiotoxicity of bupivacaine results from high lipid solubility and the R enantiomer is more toxic than the S enantiomer.

The Bupivacaine depresses the rapid phase of depolarisation (Vmax) in Purkinje fibres and Ventricular Muscle to a greater extent than lidocaine does. The CC/CNS dose ratio for Bupivacaine was 3.7±0.5.

PHARMACOKINETICS: [12]

Volume of distribution at steady state:		72 litres
Terminal elimination half life	:	210 minutes
Clearance	:	0.47 litres/minutes
Metabolism	:	Liver by dealkylation to Pipecolyloxilidine
Excretion	:	5% by the kidney as unchanged drug and the rest as metabolites.

DRUG DOSAGE: [13.14]

Plain Bupivacaine up to 2.5 mg/kg

Bupivacaine added with epinephrine-3 mg/kg.

STRUCTURE OF CLONIDINE

PHARMACOLOGY OF CLONIDINE

Clonidine hydrochloride is an imidazoline derivative with α-2 adrenergic agonist that has a variety of different actions including antihypertensive effects as well as the ability to potentiate the effects of local anaesthetic. It can provide pain relief by an opioid -independent mechanism.

MECHANISM OF ACTION: [15]

Clonidine is a selective partial α_2 adrenergic agonist with a selectivity ratio of about 200: 1 in favour of α_2 receptors. It is lipid soluble and easily penetrates the blood brain barrier to reach the hypothalamus and medulla when injected epidurally.

- It stimulates inhibitory α_2 adrenoreceptors to reduce central neural transmission in the spinal nerves.

- Inhibition of substance P release is believed to be involved in the analgesic effect.

α_2 - adrenoreceptors are located on the afferent terminals of both peripheral neurons and neurons in the superficial laminae of the spinal cord and within several brainstem nuclei implicated in analgesia.

HYPOTHESIS OF ANALGESIC ACTION OF CLONIDINE IN SPINAL CORD: [16]

The superficial laminae of the dorsal horn contain 3 groups of neurons: tonic, adapting and single-spike firing; all of which are important neuronal

structures for pain transmission, receiving most of their primary sensory input from

Aδ and C fibres. Clonidine partially inhibits voltage gated Na^+ and K^+ channels and suppresses the generation of action potentials in tonic-firing dorsal horn spinal neurons.

Some contribution to the analgesic effect of Clonidine may be through release of Ach in the neuraxial region.

PHARMACOKINETICS: [17, 18, 19, 20]

Clonidine is relatively well absorbed by most routes. Concentrations in blood peak in 2 -4 hours after oral clonidine. It is a lipid soluble drug rapidly crosses blood brain barrier. About 20 - 40% of the drug bound to plasma proteins. The volume of distribution is 150L /70 kg (2.1 ±0.4L/kg). The plasma clearance is 12.6L/hr/70 kg. 1/2 to 2/3 of an oral dose is excreted unchanged in urine, the rest as metabolites P.hydroxyclonidine. 60 -70% of the parent drug is excreted in the urine. Plasma t ½ 8-12 hrs. Effect of single dose lasts for 6 - 24 hours.

Elimination t1/2 9± 2 hrs. It is severely affected in severe renal dysfunction. (41 hour)

PHARMACOLOGICAL ACTIONS: [17, 18, 19, 20, 21]

CARDIOVASCULAR SYSTEM:

Stimulation of α_2A receptors present mainly post junctionally in medulla (Vasomotor centre) decreases sympathetic outflow leads to reduced release of norepinephrine causes fall in BP and bradycardia (also due to enhanced vagal tone). This activation of the Post synaptic α_2 adrenoreceptors in the Nucleus Tractus Solitarius and locus ceruleus of the

brain stem reduces sympathetic drive. It also activates non -adrenergic imidazoline

preferring binding sites in the lateral reticular neucleus thereby producing hypotension and an anti arrhythmogenic actions.

CENTRAL NERVOUS SYSTEM:

Being lipophilic it crosses blood brain barrier rapidly and cause analgesic action by its action with in several brain nuclei.

Sedation is a dose dependent response of clonidine by its action in the locus ceruleus

RESPIRATORY SYSTEM:

Not induce Respiratory depression even after massive overdose nor they potentiate respiratory depression from opioids.

PERIPHERAL NERVES:

Some preference over C fibres in the peripheral nerve may enhance peripheral nerve block when added to local anaesthetics

RENAL:

Dose should be adjusted according to the degree of renal impairment Decreased sympathetic flow to the kidney results in reduced renin release

PREPARATIONS AVAILABLE: [19]

Oral	0.1, 0.2, 0.3 mg tablet
IV	150 µg /ml preservative free

Transdermal patches 0.1, 0.2, 0.3 mg /24 hrs

DOSE:

For Peripheral Nerve block 1-2 µg/kg body wt [22, 23].

Intrathecally - 15-30 µg (up to 1µg/kg body weight)

Epidural dose 1-2 µg/kg bodyweight as continuous infusion

For epidural bolus dose 6-8 µg/kg bodyweight.

Intraarticular dose is 2 µg/kg bodyweight.

Oral 4-5 µg/kg

Intramuscular 2 µg/kg

Intravenous 4-8 µg/kg i.v bolus 2 µg/kg/hr continuous infusion

USE IN OBSTETRICS AND LACTATION:

Clonidine readily crosses the placental barrier and may lower the fetal heart rate. Maternal perfusion of the placenta is critically dependent on blood pressure so use of clonidine as an analgesic during labor and delivery is not indicated.

In human breast milk concentration of clonidine are approximately twice those in maternal plasma. So it is not recommended.

USE IN PAEDIATRICS:

1-2 µg/kg body weight of clonidine is administered along with local anaesthetics in caudal epidural analgesia to prolong the duration of analgesia.

USES: [19]

- As an anxiolytic/sedative

- Treatment of hypepertensive crisis.

- To prolong the duration of analgesia

  (Intrathecally/epidural/peripheral nerve blocks/ Intraarticular)

- To prevent/treat shivering

- For withdrawal from addictive drugs (Narcotics, alcohol or smoking).

- Chronic pain syndromes

- In diabetic diarrhea due to autonomic neuropathy

- Reduce menopausal hot flushes.

CONTRAINDICATIONS:

- Hypersensitivity to clonidine
- Brady arrhythmia or AV block patients
- Severe Cardiovascular diseases
- In patients with Cardiovascular/haemodynamic instability
- Pregnant/Lactating women
- Anticoagulant therapy/Bleeding diathesis

ADVERSE EFFECTS: [20]

- Hypotension may occur and usually responds to intravenous fluids, if necessary parenteral ephedrine.
- Bradycardia may occur and responds to atropine.
- Sedation which is a desirable effect.
- Mental depression, disturbed sleep.
- Dryness of mouth, nose, eyes.
- Constipation
- Confusion, headache, hyperaesthesia.
- Skin reactions (rash, urticaria and pruritus)

OVERDOSAGE:

No specific antidote for Clonidine overdosage

- Mainly supportive care
- For brady cardia Inj.Atropine will increase heart rate.
- For fall in blood pressure. Intravenous fluids and ephedrine
- An overdosage can produce Vasospasm and hypertension. For hypertensive emergency IV furosemide, diazoxide or α-blocking agents may be used.

Hypertension may develop early and may be followed by hypotension, bradycardia, hypothermia, drowsiness, irritability and miosis can occur.

STRUCTURE OF EPINEPHRINE

PHARMACOLOGY OF EPINEPHRINE: [24]

Adrenaline is an endogenous catecholamine secreted in the adrenal medulla. This is synthesised from the amino acid phenylalanine. Tyrosine hydroxylase is the rate limiting enzyme and its inhibition results in depletion of endogenous. catecholamines

Adrenaline is a direct sympathomimetic drug which act directly as agonist on α and β receptors.

Adrenaline	:	$\alpha_1+\alpha_2+\beta_1+\beta_2$ and weak β_3 action
Noradrenaline	:	$\alpha_1+\alpha_2+\beta_1+\beta_3$ but no β_2 action
Isoprenaline	:	$\beta_1+\beta_2+\beta_3$ but no α action

LOCATION OF α RECEPTORS:

α_1	-	Post Junctional on effector organ
α_2	-	Pre junctional on nerve ending (α_2A) Also post junctional in brain, pancreatic beta cells platelets and extra junctional in certain blood vessels

LOCATION OF β RECEPTORS

β_1	β_2	β_3
Heart	Bronchi, blood vessels	Adipose tissue
JG cells in Kidney	Uterus, GI tract, Urinary tract, eye	

PHARMACOLOGICAL ACTIONS

HEART:

Adrenaline increases HR by increasing the slope of slow diastolic depolarization of cells in the SA node. It also activates latent pacemakers in AV nodes and Purkinjie fibres. Arrhythmias can occur by action on α1 receptors at high doses. Refractory period of all types of cardiac cells is reduced.Cardiac Stimulations (β_1) increase rate, force and conduction velocity.

BLOOD VESSELS:

Constriction of arterioles and veins to rise in BP (mainly α_1).Dilatation of arterioles and veins fall in BP by β_2 action

RESPIRATORY SYSTEM:

Adrenaline is a potent bronchodilator (β_2).

EYE:

Mydriasis occurs due to contraction of radial muscles of iris (α_1) Intraocular pressure decreases.

GIT:

GIT relaxation occurs through activation of both α and β receptors. Peristalsis is reduced.

BLADDER:

Detrusor is relaxed (β) and trigone is constricted (α) hinders micturition. Renin release from kidney (β_1)

PERIPHERAL NERVES:

It increases the neuronal uptake of local anasthetics by decreasing the systemic absorption by its vasoconstrictive action.

UTERUS:

In Non pregnant uterus contraction (α) occurs. In term pregnant women relaxation occurs (β)

SKELETAL MUSCLE:

Neuromuscular transmission is facilitated. α receptor activation augments Ach release (α_1). Tremor occurs due to β_2 activation.

CNS:

Poorly penetrates blood brain barrier but restlessness, apprehension and tremor may occur.

METABOLIC:

Glycogenolysis,Hyperglycemia,hyperlactacidemia(β).lipolysis, Calorigenesis (β_1+β_2), Reduction of Insulin (α_2) and augmentation of glucagon (β_2) secretion.

PHYSICAL CHARACTERISTICS[25]

1 Amp: 1 ml (1:1000)

Adrenaline: 1.0 mg

METABOLISM:

Epinephrine is rapidly inactivated by the enzyme Catechol-O-Methyl transferase (COMT).

Epinephrine	→	Metaneohrine	→Conjugated Metanephrine
	MAO	MAO	MAO
3.4. dihydroxy Mandelic Acid		3 methoxy, 4 Hydroxy Mandelic acid (VMA)	3 Methoxy, 4 hydroxy Phenylglycol

Oxidative deamination by MAO also plays a part. 3methoxy4hydroxymandelic acid and metanephrine are mostly conjugated with glucuronic acid or sulfate before excretion in the urine.

PREPARATIONS AVAILABLE:

IV, IM or Sc 1 mg in 1 ml (1:1000)

0.5% by aerosol

DOSAGE: [26] In local infiltration and nerve block 1 : 2,00,000 to 1:4,00,000

IV INFUSION:

β2	1-2 µg/min.	0.02 mg/kg for Caridac collapse
β1 & β2	2-10 µg/min.	
Epinephrine		1% for bronchospasm

α1	≥ 10 µg/min.	(1g/100 ml)

USES:[24]

- Cardiac arrest
- Anaphylactic Shock
- Severe hypotension/sepsis induced hypotension
- Severe bronchial asthma
- Hay fever

ADVERSE EFFECTS: [24]

Transient restlessness, Palpitation, anxiety, tremor, pallor may occur after s.c or i.m. injection of adrenaline. Marked rise in BP, leading to cerebral haemorrhage, Ventricular tachycardia /fibrillation are due to large doses or inadvertent i.v injection.

CONTRADICTIONS: [24]

- Hypertensive Patients
- Hyperthyroidism
- In Angina Patients/severe heart diseases
- Not used along with local anaesthetics for regional blocks in finger, lips, toes.
- Along with halothane in general anaesthesia.
- Patients receiving β blockers.

REVIEW OF LITERATURE

Regional anaesthetic techniques are widely used for the provision of excellent intraoperative and post operative analgesia. Relief of post operative pain following surgery on the upper extremities can be achieved by commonly used analgesics, systemic opioids and brachial plexus block. The problem with local anaesthetic alone is that they do not provide prolonged postoperative analgesia.

Several adjuvants have been tried along with local anaesthetics to prolong the duration of post operative analgesia without the problems of prolonged motor blockade or systemic side effects.

Several studies using α_2-adrenergic agonists with bupivacaine in peripheral nerve blocks were conducted for prolongation of post operative analgesia. Initial hypothesis proposed for the mechanism of action were as follows: [34]

1. Based on the knowledge that the primary action of the α-adrenergic agonists is on the α_2-adrenoreceptors located on the afferent terminals of the peripheral neurons and neurons in the superficial laminae of the spinal cord and within several brainstem nuclei implicated in analgesia. It stimulates inhibitory α_2-adrenoreceptors to reduce neural transmission. It acts by inhibiting voltage gated Na^+ and K^+ channels and suppresses the generation of action potentials.

2. A second hypothesis may be through the release of acetylcholine. This inhibits the release of substance P in the neuraxial region. Currently

there is significant cytochemical and behavioural evidence for the existence of α_2-

adrenoreceptors.

The demonstration of α_2-adrenoreceptors in the peripheral nervous system prompted recent investigations on the use of Clonidine with local anaesthetics for regional anaesthesia procedures like brachial plexus block. Lipid solubility and the affinity of α-adrenergic agonists to their receptors seem to be important factors in determining the duration of action.

Several studies have shown that the addition of the α-adrenergic agonists to bupivacaine produces a longer period of post operative analgesia than the local anaesthetics alone.

SUBCLAVIAN PERIVASCULAR TECHNIQUE FOR BRACHIAL PLEXUS BLOCK:

1. Franco CD, Vieira ZE (2000) did a study on Subclavian Perivascular Block and its success using a nerve stimulator. They concluded that the Subclavian perivascular technique consistently provides an effective block for surgery on the upper extremity. At the site of injection the plexus is reduced to its smallest components and the sheath is reduced to its smallest volume which explains in greater part the success obtained with this block. [27]

2. Brown DL (1993) did a study on brachial plexus anaesthesia and analysed the various sites at which the plexus can be blocked. They studied the supraclavicular, interscalene, infraclavicular and axillary approaches. They concluded that the supraclavicular block produces

anaesthesia of the entire upper extremity in the most consistent and efficient manner than any other brachial plexus block technique. [28]

3. Lanz.E, Theiss D, Jankovic D (1983) studied the extent of blockade using various techniques of brachial plexus blocks. The extent of sensory and motor blockade was assessed using 0.5% bupivacaine. They concluded that the subclavian Perivascular approach of Winnie resulted in a homogenous blockade of the nerves of the brachial plexus.[29]

4. Winnie and Ramamoorthy (1977) postulated that the trunk of brachial plexus are arranged so that the central fibres are longest supplying the extremities of the limb, while the shorter fibres are arranged more peripherally as their area of supply is more proximal.

   Winnie groups the fibres into two: the Peripheral Mantle bundle which contains the outer motor and inner sensory fibres corresponding to all the early branches of the brachial plexus being motor: and a central core bundle with the outer motor fibres supplying muscles of the forearm and the inner sensory fibres carry sensation from the hand.

THUS THE ORDER OF BLOCKADE IS AS FOLLOWS:

Loss of motor power to the shoulder and upper arm; loss of sensation in the upper arm; loss of motor power of the forearm; and loss of sensation of the hand.[30]

5. Lanz.E, Theiss (1979) compared the supraclavicular and the interscalene approach of brachial plexus block. They concluded that with the Supraclavicular block, motor as well as sensory blockade of all

the nerves of the brachial plexus occurred with about the same frequency. Following both the techniques, blockade developed from the proximal to distal with motor blockade preceding the sensory block.[31]

6. Cheryl etal[32] did a comparative study with 0.25% bupivacaine and 0.25% ropivacaine in the brachial plexus. They concluded that both groups required supplementation with peripheral nerve blocks or general anaestheia in a large number of cases. In view of the frequent need for supplementation with both 0.25% bupivacaine and 0.25% ropivacaine they do not recommend using the 0.25% concentrations of these local anaesthetics to provide brachial plexus block.

CLONIDINE IN BRACHIAL PLEXUS BLOCK WITH LOCAL ANAESTHETICS:

1. Erlacher W et al (2001) evaluated the efficacy of adding clonidine to mepivacaine, Ropivacaine and bupivacaine in axillary perivascular brachial plexus blcok by comparing 3 groups. They concluded that the onset of sensory block with mepivacaine is faster than Ropivacaine and bupivacaine but the duration of motor blockade and sensory blockade was prolonged by Clonidine in the mepivacaine and bupivacaine groups.[33]

2. Castia A.et al conducted a double blind study for improving postoperative analgesia after axillary brachial plexus anaesthesia with 0.75% ropivacaine with 1 µg/kg of Clonidine in two groups, each with 15 patients. By adding 1 µg/kg of Clonidine to 20 ml of ropivacaine 0.75% for axillary brachial plexus anaesthesia, a 3 hour delay in first

analgesic request postoperatively without clinically relevant effects on the degree of sedation and cardiovascular homeostasis was observed.[34]

3. Salvatore sia and Antonella Lepri (1999) conducted a double blinded study to determine whether Clonidine has analgesic effects when administered into the brachial plexus sheath. They concluded that Clonidine prolongs the analgesic

effects of brachial plexus block when mixed with local anaesthetic bupivacaine. Anesth analog 1999:88:1109-1112.[35]

4. E1 Saied AH et a1 conducted a randomised double blinded placebo controlled study using Clonidine 150 µg in 40 ml of 0.75% Ropivacaine. Control group received 1 ml NS to the 0.75% Ropivacaine. The results showed an increase in duration of sensory and motor block and duration of analgesia without an increased incidence of side effects in the clonidine group compared to the control group. [36]

5. Hutschala et al in 2004 conducted the study by adding Clonidine to local anaesthetics bupivacaine 0.25%. They found that addition of Clonidine to local anaesthetics enhances pain relief after peripheral nerve block. Lower clonidine plasma concentration after peripheral nerve blockade strongly suggest a local effect. Administration of Clonidine was associated with sedation and a decrease in heart rate and blood pressure independent of the route of administration. [37]

6. Duma et al in 2005 conducted a randomised controlled study in axillary brachial plexus block. Using Clonidine as an adjuvant to local anaesthetic four groups of 20 patients in each group were investigated

using i) 40 ml of 0.5% levobupivacaine plus 150 µg of Clonidine ii) 40 ml of levobupivacaine 0.5% plus 1 ml of 0.9% Nacl iii) 40 ml of bupivacaine 0.5% plus 150 µg clonidine. iv) 40ml of bupivacaine 0.5% plus 1 ml of NaCl 0.9% respectively. The onset of motor and sensory block and duration of sensory block were recorded. They found that there is no significant difference between groups but a significantly higher variance ($P<0.001$) was found in the two groups with Clonidine than in the two groups without. These finding suggest responder and nonresponder behaviour is a result of the addition of clonidine. [38]

7. Adnan T et al (2005) conducted a double blind controlled study on 28 adult chronic renal failure patients. The control group received 40 ml of lignocaine 1% combined with 1 ml of NS and the clonidine group received 40 ml of lignocaine 1% with 150 μg of Clonidine. They concluded that onset time for sensory blockade was longer in the Clonidine group than in the controls (P=0.013) and both motor and sensory blocks lasted longer in the Clonidine group (P=0.004, P<0.001, respectively). In addition, the Clonidine group had lower mean arterial pressures, heart rates and higher sedation scores compared to the control (P<0.05 for all).[39]

CLONIDINE IN OTHER REGIONAL ANAESTHETIC PROCEDURES

1. Filos KS et al in 1994 evaluate the dose response haemodynamic and analysis profiles of intrathecal clonidine in a randomized prospective study. The study concluded that there is a dose dependent analysis after intrathecal clonidine. At 300 and 450 micro gram intrathecal clonidine a relative haemodynamic stability is observed [40]
2.
3. Filos KS et al, Conducted a double blind placebo controlled study to evaluate the efficacy of intrathecal clonidine on pain following LSCS under general anaesthesia. The results suggest that intrathecal clonidine 150 micro grams is effective in controlling pain following caesarean section but may cause side effects such as hypotension, sedation and dryness of mouth [41]
4. Huang Y et al, done a randomised dose ranging study in eighty ASAI-III patients to determine the optimal epidural dose of clonidine to provide the best analgesia with

fewest side effects. He concluded that the groups receiving clonidine experienced less post operative pain (P= 0. 002) [42]

5. Upadhyay P and Handa H studied the duration of analgesic action and incidence of side effects of clonidine added to bupivacaine given caudally in a 50 paediatric patients. They concluded that the addition of clonidine in the dose of 1 micro gram/Kg to bupivacaine (0.25%) 0.75 ml/kg for caudal blockade significantly prolongs the duration of analgesia without any side effects. [43]

6. Gentili M et al, done a prospective comparative study in a group of 40 patients to assess the potential analgesic effect of clonidine after intra articular administration. They concluded that low dose of intra articular clonidine produces analgesia unrelated to vascular uptake of the drug. [44]

MATERIALS AND METHODS

This study was carried out in the plastic and orthopaedic surgery theatre, Government General Hospital, Chennai after obtaining institutional approval. The aim of the study was to evaluate the efficacy of blocking the brachial plexus with bupivacaine and the effects of added alpha adrenergic agonists like clonidine and epinephrine.

STUDY DESIGN:

A prospective, randomised study conducted on 40 ASA I and II patients undergoing upper limb surgeries under supraclavicular brachial plexus block who fulfil inclusion criteria

The study was started after receiving institutional ethical committee approval and informed written consent from all the patients and they were randomly divided into two groups.

TWO GROUPS:

BA -30ml of 0.375% bupivacaine with 5 μg/ml of epinephrine.
BC -30ml 0f 0.375% bupivacaine with 1 μg/kg of clonidine**.**

Inclusion criteria:

The following criteria were taken for including the patients in this study.

- ASA Status I and II
- Age between 18 and 65 years
- Weight >50 kg
- Patients undergoing surgery of upper limb with possibility of shoulder abduction for assessment of motor blockade.

Exclusion criteria:

- Patient refusal
- Known allergy for the drugs to be studied.
- Local infections / Sepsis
- Coagulation abnormalities
- H/o significant neurological, psychiatric , neuromuscular, cardiovascular, pulmonary, renal or hepatic disease
- Alcohol/drug abuse
- Pregnancy/lactating women
- Chronic analgesic therapy (other than NSAIDS)
- On adrenergic drugs
- Peripheral neuropathy
- Not fulfilling inclusion criteria

MATERIALS:

1. Sterile tray for regional blocks
2. Drugs for the block

    0.5% bupivacaine

    Inj.Clonidine

    Inj.Epinephrine

    Normal saline

3.

4. Nerve stimulator with insulated needle

5. Equipments and drugs for resuscitation

6. Equipments and drugs for conversion to general anaesthesia in the case of block failure

METHODS:

PRE OPERATIVE PREPARATION:

Patients were pre-operatively assessed and the procedure was explained to the patient. Written informed consent was obtained. They were assessed with particular attention to any contraindications.

Assessment of pain using Visual Analogue Scale (VAS) post operatively was explained to the patient pre operatively**.**

PRE MEDICATION:

Tab.ranitidine 150mg 2 hours before surgery with sips of water.

CONDUCT OF ANAESTHESIA:

On arrival of the patient in the operating room, monitors like pulse oxymeter, non invasive blood pressure and ECG were connected and baseline values were recorded. An intravenous access was obtained in the opposite arm.

SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK BY THE SUBCLAVIAN PERIVASCULAR TECHNIQUE[7]

Patients were positioned supine with the head turned away from the side to be blocked and the ipsilateral arm adducted. The neck was prepared with povidone iodine solution

and draped with sterile towels.

LANDMARKS:

The essential landmarks to be identified are

1. Cricoid cartilage
2. Interscalene groove
3. Clavicle midpoint
4. Subclavian artery

PROCEDURE: FIG - 6

A line was drawn laterally from the cricoid cartilage to cross the sternomastoid at its midpoint. The interscalene groove was located behind the midpoint of the posterior border of the muscle. To confirm this position the middle and anterior and middle scalene muscles were made prominent by asking the patient to inspire vigorously or sniff. The interscalene groove was then followed distally towards the clavicle. Approximately 1 to 1.5 cm above the midpoint of the clavicle, the pulsation of the subclavian artery was made out in the interscalene groove.

Under strict aseptic precautions standing by the side of the patient, the interscalene groove was palpated with the index finger, reversing the hands for the opposite side. Patient placed supine with head turned away from the side to be blocked and ipsilateral arm adducted, the interscalene groove and the midpoint of clavicle identified. After local infiltrations of 1 ml of 2% lignocaine intradermally in the interscalene groove 1 to 1.5 cm above the clavicle, a 22G, 50 mm short bevelled unipolar insulated needle connected

to a nerve locator is directed caudally towards the ipsilateral nipple and posteriorly. End point in a nerve stimulator is a motor response with an output lower than 0.5mA. to

avoid intra vascular injection aspiration done every 3-5 ml of study drug injected.

EVALUATION OF THE BLOCK:

The following observations were made.

- Vital signs monitoring; heart rate, non invasive blood pressure, oxygen saturation and sedation score were measured every minute for the first 5minutes and every 5 minutes thereafter until the end of surgery. For statistical purposes, they were documented at 0, 1, 2, 5, 10, 15, 30 minutes and every 30 minutes thereafter.
- Immediately following the administration of the drug, patients were evaluated for the onset of sensory and motor blockade every minute.
- Sensory block evaluated by temperature sensation using ether soaked cotton in the skin dermatomes C4-T2.
- Onset of motor blockade was assessed by loss of shoulder abduction. Only patients with complete motor block are included in the study. Failure of the block to be established even after 20 minutes was taken as block failure.
- Analgesic failure were managed with local anaesthetic supplementation or General anaesthesia as appropriate .Those patients are excluded from the study.
- After confirmation that the block has taken up, surgery was started.
-
- Patient receiving supplemental O2 and intravenous fluids throughout the procedure
- Sedation is assessed using Ramsay sedation score (6 points). If the patient is anxious even 1 hour after blocking the plexus, inj.Midazolam was given to achieve a sedation score of 2 to 3.

- Local anaesthetic toxic reactions including subjective and objective manifestations like circumoral numbness, tinnitus, twitching, convulsions, etc., were looked for and appropriate measures were taken.
- Complications associated with the technique like intravascular injection, intrathecal or epidural injection and pneumothorax were looked for and appropriate measures were taken to meet any such eventuality.
- Postoperatively heart rate, non invasive blood pressure, oxygen saturation and sedation scores are recorded at 0 min, 30 min, 60 minutes, 2 hr, 4 hr, 6 hr, 12 hr and 24 hr.
- Duration of sensory block (time elapsed between injection of the drug and appearance of pain in the surgical site).
- Duration of sensory blockade was tested postoperatively using the VAS score every ½ hour for the first six hours thereafter every 2 hours till 24 hours. VAS scale (0-10points), where 0 represents no pain and 10 means worst possible pain.
- Pentazocine 30 mg intramuscularly is given as a rescue analgesic when the pain score is more than 4.

SIDE EFFECTS LOOKED FOR 24 HOURS:

a. Bradycardia; heart rate less than 60 beats per minute.

b. Hypotension; more than 30% decrease from baseline value.

c. Sedation

d. Shivering

e. Dry mouth

f. Arrhythmias

g. Local anaesthetic toxicity

All the data were subjected to statistical analysis. The parameters of age and sex were analysed using Chi-square test. Onset time for motor and sensory blockade, duration of surgery and duration of sensory blockade were analysed with LEVENE's Test and t-test and the statistical significance estimated. A P value less than equal to 0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

The patients included in this study were divided into two groups consisting of 20 patients each.

Group BC (n=20) received 30ml of 0.375% bupivacaine with 1 micro gram/kg of clonidine.

Group BA (n=20) received 30ml of 0.375% bupivacaine with 5 micro gram/ml of epinephrine.

AGE

MEAN AGE IN YEARS IN THE TWO GROUPS STUDIED

Group	*N*	*Mean(years)*	*Median*	*S.D*
BA	20	32.50	27.50	12.89
BC	20	32.05	28.00	11.26

STATISTICAL ANALYSIS OF AGE DISTRIBUTION

	df	*F*	*p Value*
Chi-Square test	38	0.275	0.541

GE RANGE GROUP CROSS TABULATION

Age Range		*Group*		*total*
		BA	*BC*	
< 30 years	Count	11	12	23
	% With in age range	47.8%	52.2%	100.0%
30-40 years	Count	5	4	9
	% With in age range	55.6%	44.4%	100.0%

40-50 years	Count	1	3	4
	% With in age range	25.0%	75.0%	100.0%
50-60 years	Count	3	1	4
	% With in age range	75.0%	25.0%	100.0%
Total	Count	20	20	40
	% With in age range	50.0%	50.0%	100.0%

Thus as the two groups were similar with respect to age distribution the difference was not statistically significant.

WEIGHT

MEAN WEIGHT IN KGS IN THE TWO GROUPS STUDIED

	N	*Mean (Kgs)*	*SD*
Group BA	20	60.90	7.84
Group BC	20	64.30	8.29

STATISTICAL ANALYSIS OF WEIGHT DISTRIBUTION

Levene's test		*t test for equality of means*		
F	***Siqnificant***	***t***	***df***	***p Value***
.612	.439	-1.333	38	.191

There was no statistically significant difference among the two groups with respect to weight distribution.

SEX

SEX DISTRIBUTION IN THE TWO GROUPS STUDIED

	Value	*df*	*p Value*
Chi-square	0.784	1	0.376

There was no statistically significant difference among the two groups as regards sex distribution.

TYPE OF SURGICAL PROCEDURE

Procedures	*Group BA*	*Group BC*
ORIF	12	9
Posttraumatic Deformity	4	2

correction		
EF	1	4
Radial head excision	1	2
Sequestrectomy & IF	1	1
Implant exit	1	1
Tension band wiring	1	1

ORIF - Open Reduction and Internal Fixation
IL - Interlocking
EF - External Fixation
AE - Above Elbow

The two groups were well matched for the type of surgical procedure suggesting postoperative pain of similar intensity.

Duration of surgery in minutes
mean duration of surgery in the two groups

Group	*N*	*Mean (minutes)*	*SD*
BA	20	102.75	22.56
BC	20	109.00	21.74

STATISTICAL ANALYSIS OF DURATION OF SURGERY

Levene's test		*t test for equality of means*		
F	***Significant***	***t***	***df***	***p Value***
.000	.985	-.892	38	.378

The duration of surgery in the groups was not statistically significant.

ONSET OF SENSORY BLOCKADE IN MINUTES

MEAN ONSET OF SENSORY BLOCK IN THE TWO GROUPS

Group	*N*	*Mean(minutes)*	*SD*
BA	20	6.25	1.33
BC	20	5.85	1.27

STATISTICAL ANALYSIS OF ONSET OF SENSORY BLOCKADE

Levene's test		*t test for equality of means*		
F	***Significant***	***t***	***df***	***p Value***
.156	.695	.972	38	.337

Onset of sensory blockade in the two groups was comparable and there was no statistically significant difference among the two groups.

Onset of motor blockade in minutes

MEAN ONSET OF MOTOR BLOCK IN THE TWO GROUPS

Group	*N*	*Mean(minutes)*	*SD*
BA	20	3.80	.834
BC	20	3.55	1.05

STATISTICAL ANALYSIS OF ONSET OF MOTOR BLOCKADE

Levene's test		*t test for equality of means*		
F	***Significant***	***t***	***df***	***p Value***
1.428	.240	.834	38	.410

The two groups did not show any statistical significance with respect to the time for onset of motor blockade.

DURATION OF SENSORY BLOCKADE IN HOURS

MEAN DURATION OF SENSORY BLOCKADE

Group	*N*	*Mean(Hours)*	*SD*
BA	20	7.12	.63
BC	20	12.69	1.28

STATISTICAL ANALYSIS OF DURATION OF SENSORY BLOCKADE

Levene's test		*t test for equality of means*		
F	***Significant***	***t***	***df***	***p Value***
9.786	.003	-17.398	38	.001

Intra Operative Pulse Rate

Intra Operative Systolic BP Trend

ntra Operative Diastolic BP Trend

Post Operative Pulse Trend

Post Operative Systolic Bp Trend

Post Operative Diastolic Bp Trend

Patients in group BC had a longer duration of sensory blockade than patients in group BA and the difference was statistically significant.

HEMODYNAMIC PARAMETERS

There was no significant difference in the vital signs like heart rate, systolic blood pressure, diastolic blood pressure and saturation (SPO_2) from the baseline throughout the surgery and the post operative period of 24 hours in the two groups.

SIDE EFFECTS

None of the patients in the two groups developed any of the side effects like bradycardia, hypotension, sedation, dry mouth, dizziness, arrhythmias and local anaesthetic toxicity.

DISCUSSION

The subclavian perivascular approach to the brachial plexus with the guidance of nerve locator has gained popularity because of satisfactory anaesthesia and a decreased failure rate with this approach.

Franco CD Vieira ZE [27] in their study on subclavian perivascular brachial plexus block found that the subclavian perivascular block provides an effective block for surgery on the upper extremity. Brown[28] in his study on analysis of options in brachial plexus anaesthesia concluded that the supraclavicular block provides anaesthesia of the entire upper extremity in the most consistent and time efficient manner compared to other techniques. Lanz[29] and his colleagues in their study on the extent of blockade following various techniques of brachial plexus block demonstrated that the subclavian perivascular approach to the brachial plexus resulted in a homogenous blockade of the nerves of the brachial plexus.

With the supraclavicular approach injection is made at the level of the trunks. As there are only three components at this level, failure rates should be extremely low. With the supraclavicular technique incidence of pneumothorax is 0.5-6% which is usually asymptomatic.

Therefore in this study the subclavian perivascular approach to the brachial plexus was used.

Cherryl et al [32] in their comparative study of 0.25% bupivacaine and 0.25% ropivacaine for brachial plexus block demonstrated a higher incidence of supplementation required. Therefore they recommended using

local anaesthetics of concentration more than 0.25% to provide brachial plexus block. Therefore, in this study 0.375% bupivacaine is used.

According to Denise J.Wedel in the subclavian perivascular technique the solution is delivered at a point in which the trunks are compactly arranged. So a volume of 20-30ml of local anaesthetic solution is sufficient. Therefore in this study a volume of 30ml was used.

The demonstration of α2 receptors in the peripheral nervous system prompted recent investigations on the use of α2 receptor agonists either alone or combined with local anaesthetics for regional anaesthesia procedures like brachial plexus block. Several studies have shown that the addition of α2 agonist clonidine with bupivacaine produces a longer duration of post operative analgesia.

In this study, the alpha agonists like clonidine or adrenaline were added as an adjuvant to bupivacaine in brachial plexus block and their effects were evaluated. In the study by Jean J. Eledjam MD and his colleagues[46] the mean weight of patients was 64.03 ± 2.2kg in clonidine with bupivacaine group and 66.3 ± 2kg in adrenaline with bupivacaine group.

In this study, the mean weight of patient in group BC was 64.30 ± 8.29kg and in group BA was 60.90 ± 7.84kg

DOSAGE OF ALPHA AGONISTS

In the study by Castia et al[34] adding 1 micro gram/kg of clonidine to local anaesthetics for brachial plexus block provided a prolonged duration of sensory analgesia postoperatively without clinically relevant effects on
the degree of sedation and cardiovascular homeostasis. Therefore in this study clonidine was used on a weight basis 1 micro gram/kg.

In the study by Eledjam JJ et al[46] adrenaline 150 micro gram was added to 30 ml of bupivacaine (i.e 5µg/ml) to find the efficacy of alpha agonist on the brachial plexus block. So in our study adrenaline 5µg/ml was added to local anaesthetic and compared with α2 receptor agonist clonidine.

ONSET OF SENSORY BLOCKADE

The onset of sensory analgesia was tested by temperature testing using ether soaked cotton in the skin dermatome C4-T2. In this study the time for onset of sensory analgesia was 6.25 ± 1.33 minutes in group BA and 5.85 ± 1.26 minutes in group BC. The difference was not statistically significant among the two groups. In the study by

Eledjam and his colleagues[46] there was no difference in onset time of sensory blockade between clonidine and adrenaline group.

ONSET OF MOTOR BLOCKADE

The onset of motor blockade was tested by loss of shoulder abduction. In this study the onset time for motor blockade was 3.80 ± 0.834 minutes in group BA and 3.55 ± 1.05 minutes in group BC. The difference was statistically insignificant among the two groups. The finding that motor blockade develops before sensory blockade is consistent with the study by Winnie and Ramamoorthy[30]. In the study by Eledjam and his colleagues[46] there was no difference in the onset of motor blockade between the two group's clonidine with bupivacaine and adrenaline with bupivacaine. In another study by EL Saied AH[36] and colleagues there was no difference in onset time of motor block between the clonidine groups and control groups.

DURATION OF ANALGESIA

In our study the duration of sensory block in group BA was found to be 7.12 ± 0.63 hours and for group BC 12.69 ± 1.28 hours. Thus the addition of clonidine to bupivacaine prolongs the duration of analgesia significantly than the bupivacaine with adrenaline group.

In the study by Eledjam JJ[46] and colleagues the addition of 150 µg clonidine with 0.5% bupivacaine conferred a mean duration of postoperative analgesia of 994.2 ± 34.2 minutes compared with 728.3 ± 35.8 minutes for 150µg of adrenaline with 0.5% bupivacaine.

In the study by Casati A et al[34] the addition of clonidine provided 15.2 hours of postoperative analgesia. In the other study by EL Saied AH et al[36] the addition of clonidine showed a duration of sensory analgesia from 587 minutes to 828 minutes.

In the study by Erlacher et al[33] the addition of 150µg of clodinine to 40ml of 0.5%

bupivacaine prolonged the duration of sensory blockade to 972±72 minutes.

In the other study by Adnan T and colleagues[47] the addition of clonidine to local anaesthetics prolongs the duration of sensory block significantly with the P value < 0.001.

In the study by Duma A and colleagues, findings suggest higher variance in the duration of sensory block within the clonidine group. They concluded the study by saying there is a responder and non responder behaviour within the patients in the clonidine group.

HAEMODYNAMIC PARAMETERS

In this study there was no significant change in the haemodynamic parameters from the baseline in both the groups.This was consistent with the observation by EL Saied AH et al[36]. Eledjam JJ et al[46] and Casati A et al[34].

In the study of 28 adult chronic renal failure patients by Adnan T et al [47] addition of clonidine in brachial plexus block decreases both heart rate and blood pressure.

SIDE EFFECTS

None of the patients in the two groups showed any of the side effects like bradycardia, hypotension, sedation, dry mouth, dizziness, arrhythmias and local anaesthetic toxicity.

In the study by Eledjam JJ and Colleagues [46] in 1991 none of the patients reported clonidine related side effects. In another study performed by Casati A in 2001 [34], no significant clonidine related side effects like sedation or haemodynamic instability when added to the local anaesthetic was observed. This was consistent with the observation by EL Saied AH and colleagues [36].

But in the study of 28 adult chronic renal failure patients by Adnan T et al [47] in 2005 showed that the clonidine group had lower mean arterial pressure, heart rate and higher sedation score compared to the control groups.

SUMMARY

On comparing the effects of added alpha adrenergic agonists clonidine and epinephrine to bupivacaine for supraclavicular brachial plexus block, it was found that

- Onset of sensory blockade was similar in the two groups.
- Onset of motor blockade was similar in the two groups.
- Duration of sensory blockade was significantly longer in the clonidine with bupivacaine group compared with the epinephrine with bupivacaine group.
- There was no significant difference in the haemodynamic parameters between the two groups.
- No clonidine or epinephrine related side effects were recorded in the groups.
- No other complications were seen in the two groups.

CONCLUSION

From this study it can be inferred that the addition of clonidine to 0.375% bupivacaine prolonged the duration of analgesia significantly when compared to epinephrine added to 0.375% bupivacaine.

In conclusion the addition of 1μg/Kg of clonidine to 0.375% bupivacaine in supraclavicular brachial plexus block provides a significant advantage over 5μg/ml of epinephrine to 0.375% bupivacaine in terms of postoperative analgesia without any significant side effects.

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PATIENT PROFORMA

Name: Informed written Consent:
Age: Diagnosis:
Sex: Surgery:
ASA: Weight:
MPC: Comorbid Conditions:

INVESTIGATIONS:

Hb BT CT

MONITORS:

HR NIBP Sa02

GROUPS:

BC

BA

BLOCK CHARACTERISTICS:

	Time of Injection	Time of onset	Time Elapsed
Sensory Block			
Motor Block			

INTRAOPERATIVE HAEMODYNAMICS:

Time
HR
BP
Sa02
Sedation Score
0 Min

1 Min

2 Min

3 Min

4 Min

5 Min

10 Min

15 Min

20 Min

25 Min

30 MIn

35 Min

40 Min

45 Min

50 Min

55 Min

60 Min

POSTOPERATIVE HAEMODYNAMICS:

Time	HR	BP	Sa02	Pain Score	Sedation Score
0 Min					
15 Min					
30 Min					
1 Hr					
2 Hr					
3 Hr					
4 Hr					
6 Hr					

12 Hr

24 Hr

Time of first appearance of pain at surgical site Total Duration Of sensory Block

PERIOPERATIVE COMPLICATIONS:

	Intra Operative	Post Operative	Treatment Given
Local Toxicity			
Bradycardia			
Hypotension			
Shivering			
Dry Mouth			
Arrhythmias			
Headache			
Dizziness			

S.No	Age	weight in kg	sex	duration of surgery in minutes	onset of sensory block in minutes	onset of motor block in minutes	duration of sensory block in hours
1	60	50	F	140	5	4	7.25
2	18	55	F	70	4	3	6.5
3	32	70	M	100	7	4	7.25
4	18	56	M	100	6	4	7.5
5	23	63	M	80	5	3	6.5
6	26	55	M	90	4	3	7
7	38	60	M	80	6	2	7.25
8	23	56	M	95	5	3	7.5
9	40	80	M	120	7	4	7.5
10	31	60	M	130	6	4	7.25
11	45	50	F	160	7	5	7.5
12	25	60	M	90	5	3	6.5
13	38	65	M	90	6	4	6.5
14	27	60	M	80	5	3	6.5
15	32	70	M	110	7	4	7.25
16	28	60	F	80	5	3	6.25
17	23	55	M	100	7	4	7.25
18	21	60	M	110	6	3	6.5
19	35	60	M	140	7	4	7.25
20	25	70	M	90	6	3	7.5

Bupivacaine with clonidine - group BC

S.No
Age
weight in kg
sex
duration of surgery in minutes
onset of sensory block in minutes
onset of motor block in minutes
duration of sensory block in hours

1
45
75
M
130
5
3
13.15
2
40
60
M
100
4
2
12.25
3
50
78
M

140
5
3
14.3
4
25
60
M
140
6
3
15.45
5
28
70
M
80
3
2
12.1
6
28
75
M
120
5
3
11.3
7
38
75
M
90
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4
14
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20
60
M
60
8

6
11.15
9
18
54
M
100
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12.45
10
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60
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11.3
11
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55
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120
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3
12.15
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13.3
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20
64
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12.3
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F
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Intra operative Pulse Chart - Group BA

s.no
0 min
1 min
2 min
5min
10 mins
15 mins
30 mins
60 mins
90 mins
120 mins
1
88
88
89
86
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86
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94
90
2
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86
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88
77
77
76
3
88
88
90
90
86
87
90
92
84
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4
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80
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89
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Intra operative Pulse Chart - Group BC

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10 mins
15 mins
30 mins
60 mins
90 mins
120 mins
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Intra operative systolic BP Chart - Group BA

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2 min
5 min
10 mins
15 mins
30 mins
60 mins
90 mins
120 mins
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Intra operative systolic BP Chart - Group BC

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2 min
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10 mins
15 mins
30 mins
60 mins
90 mins

120 mins
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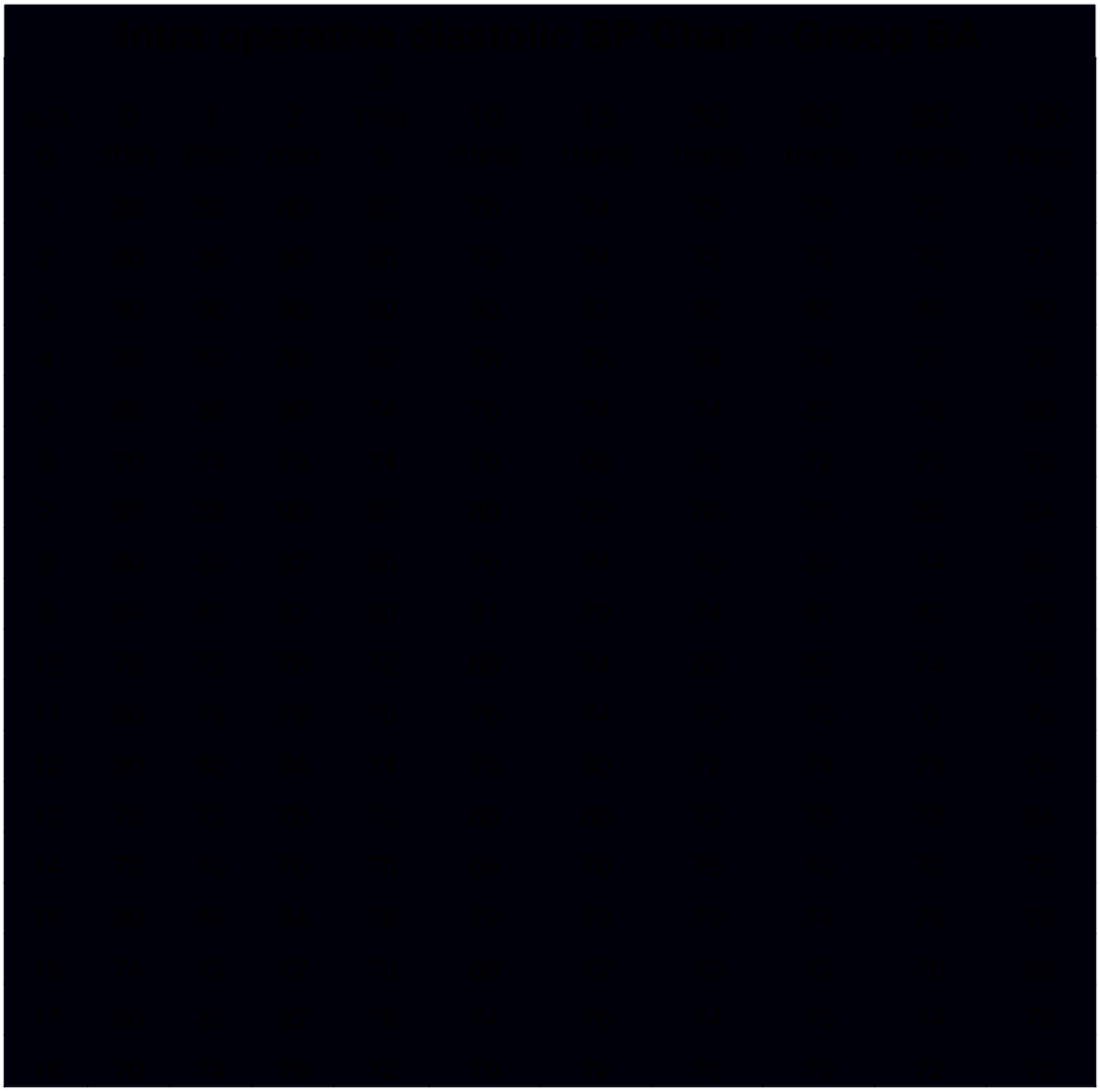
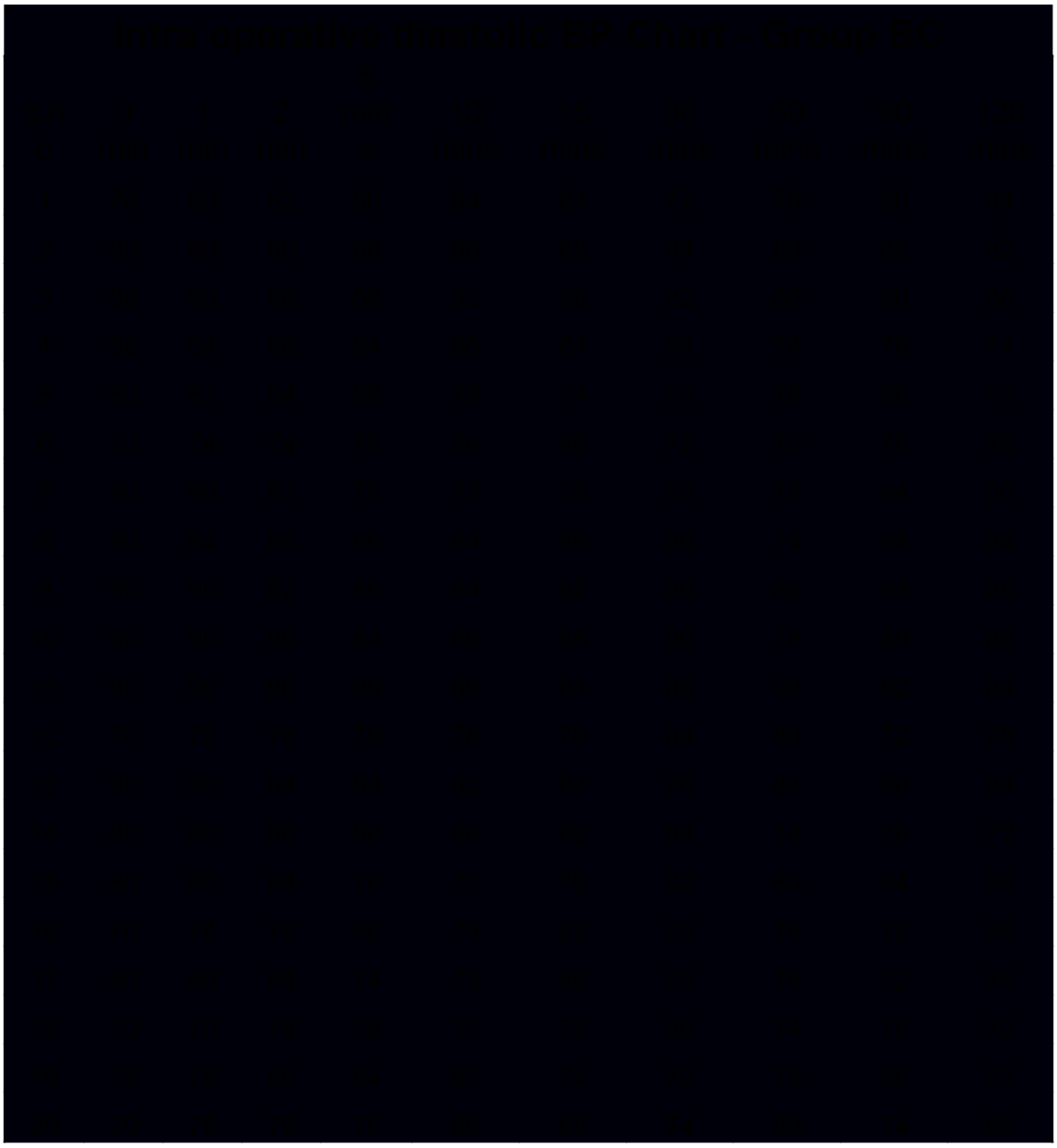
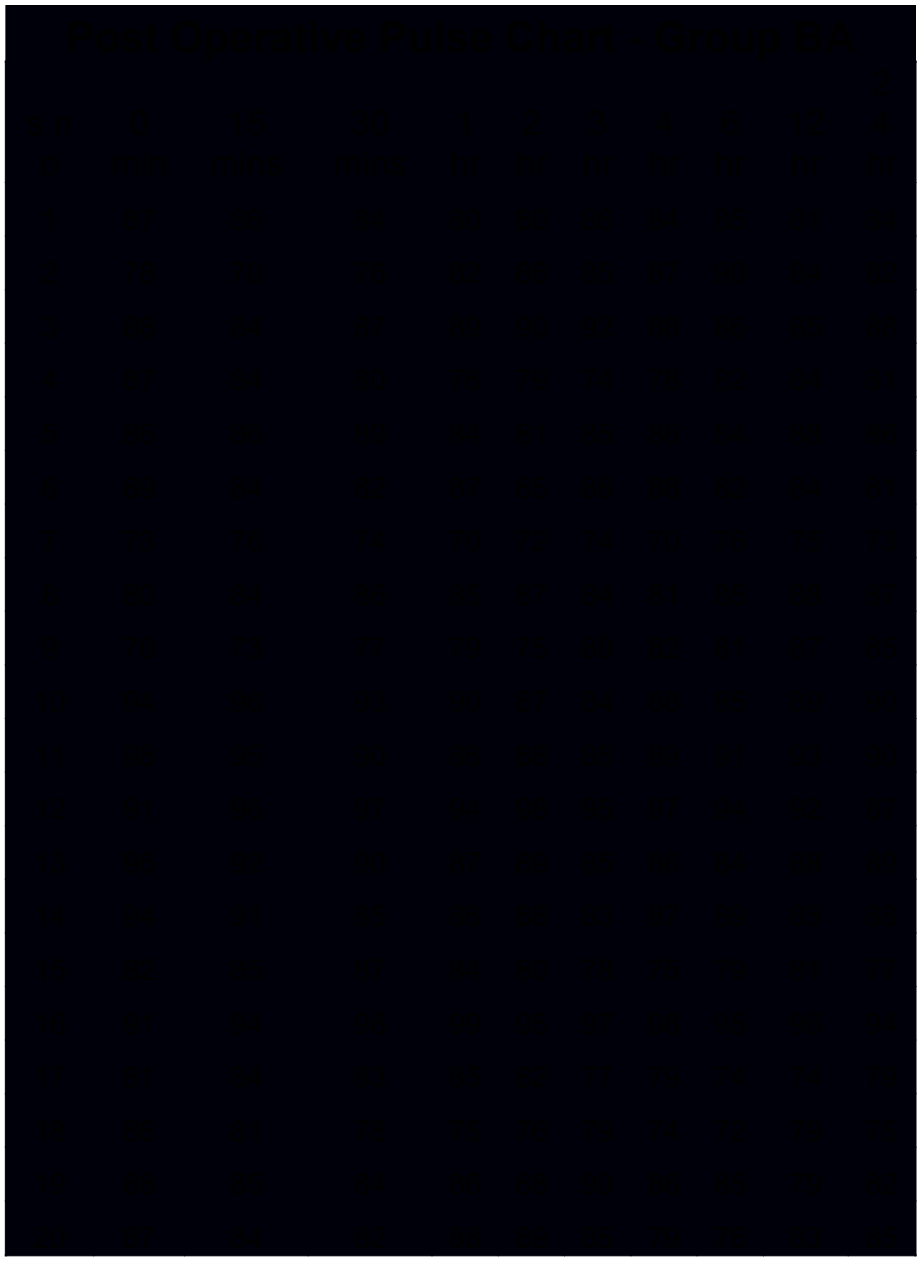
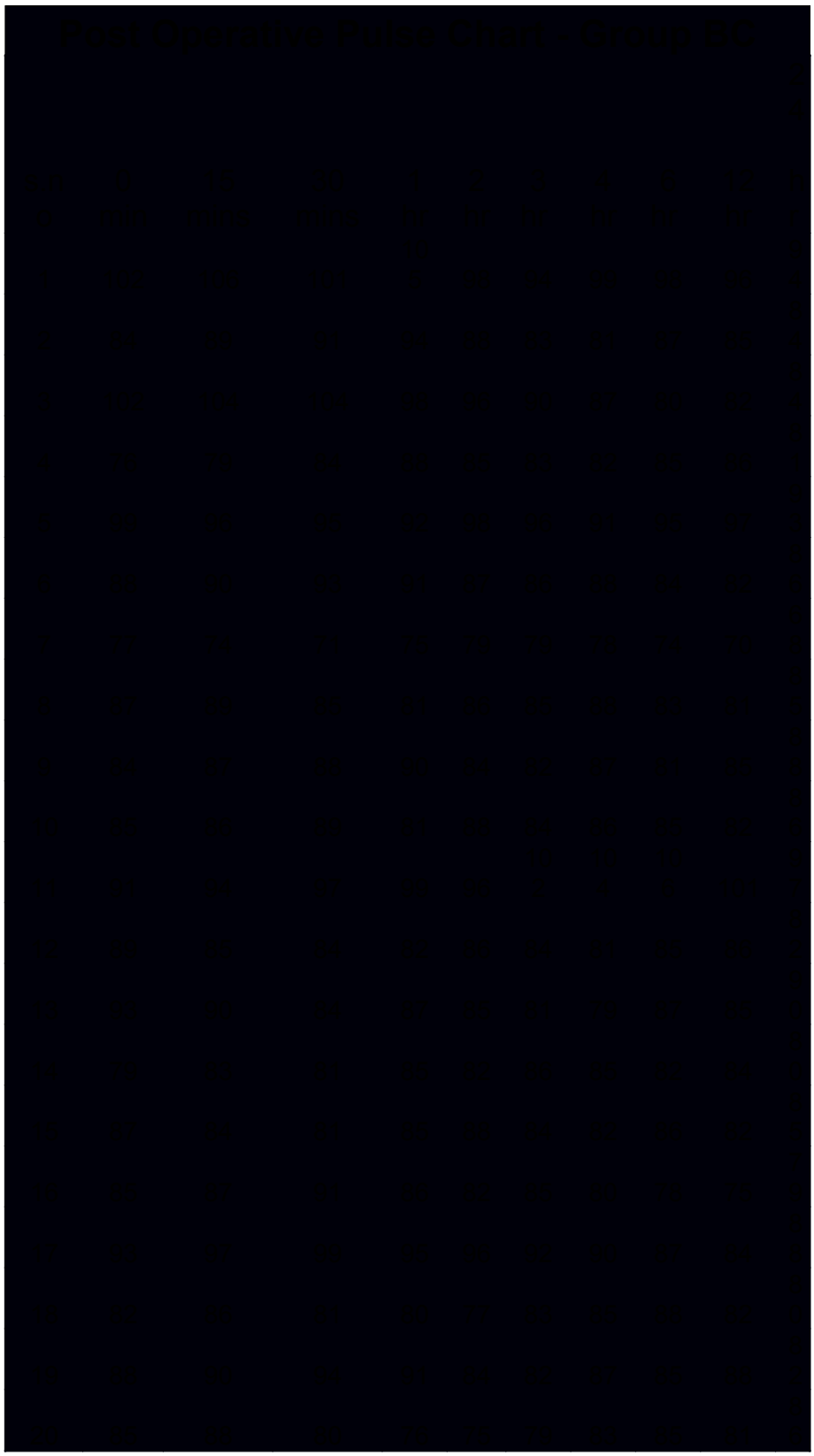
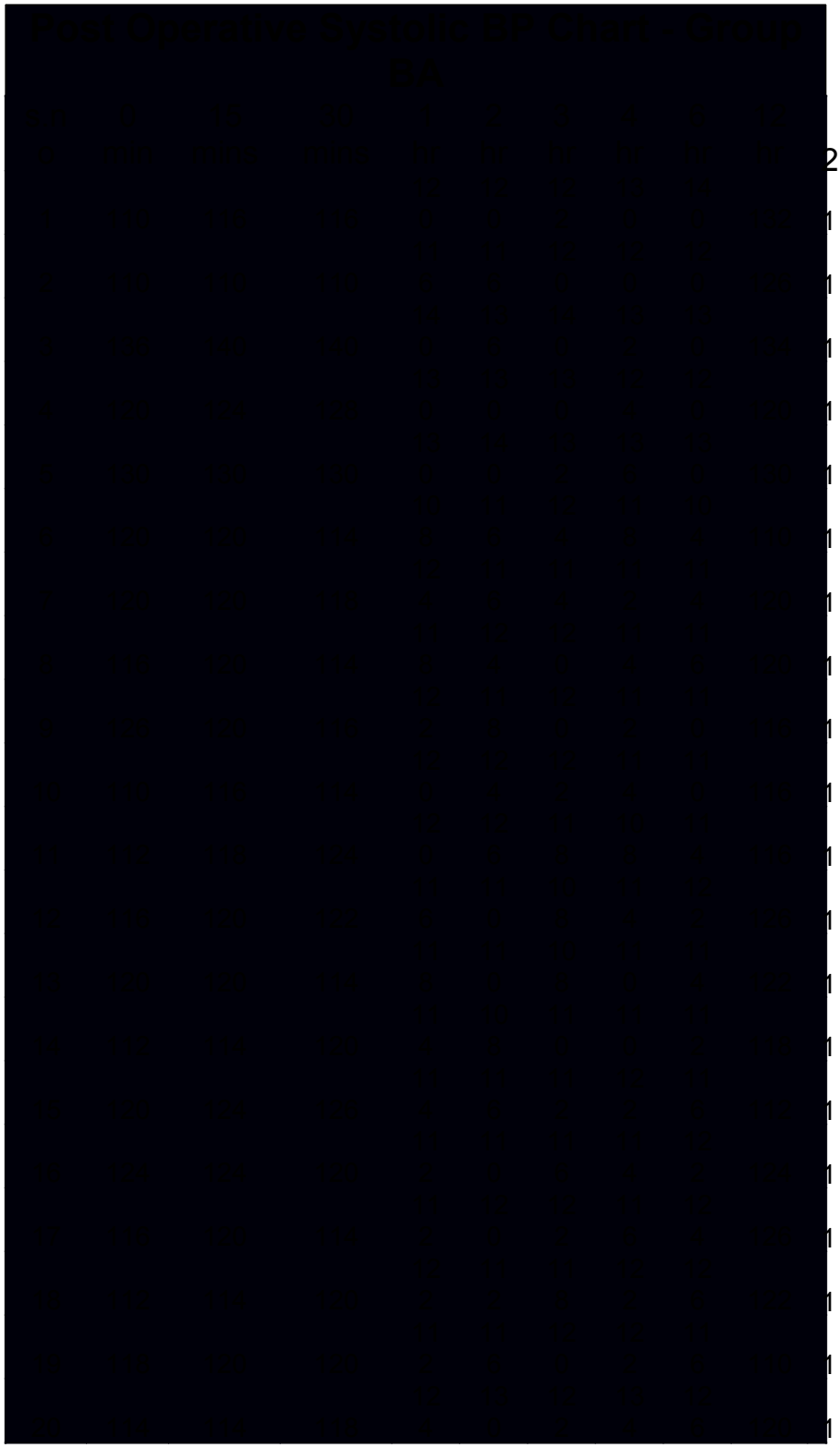
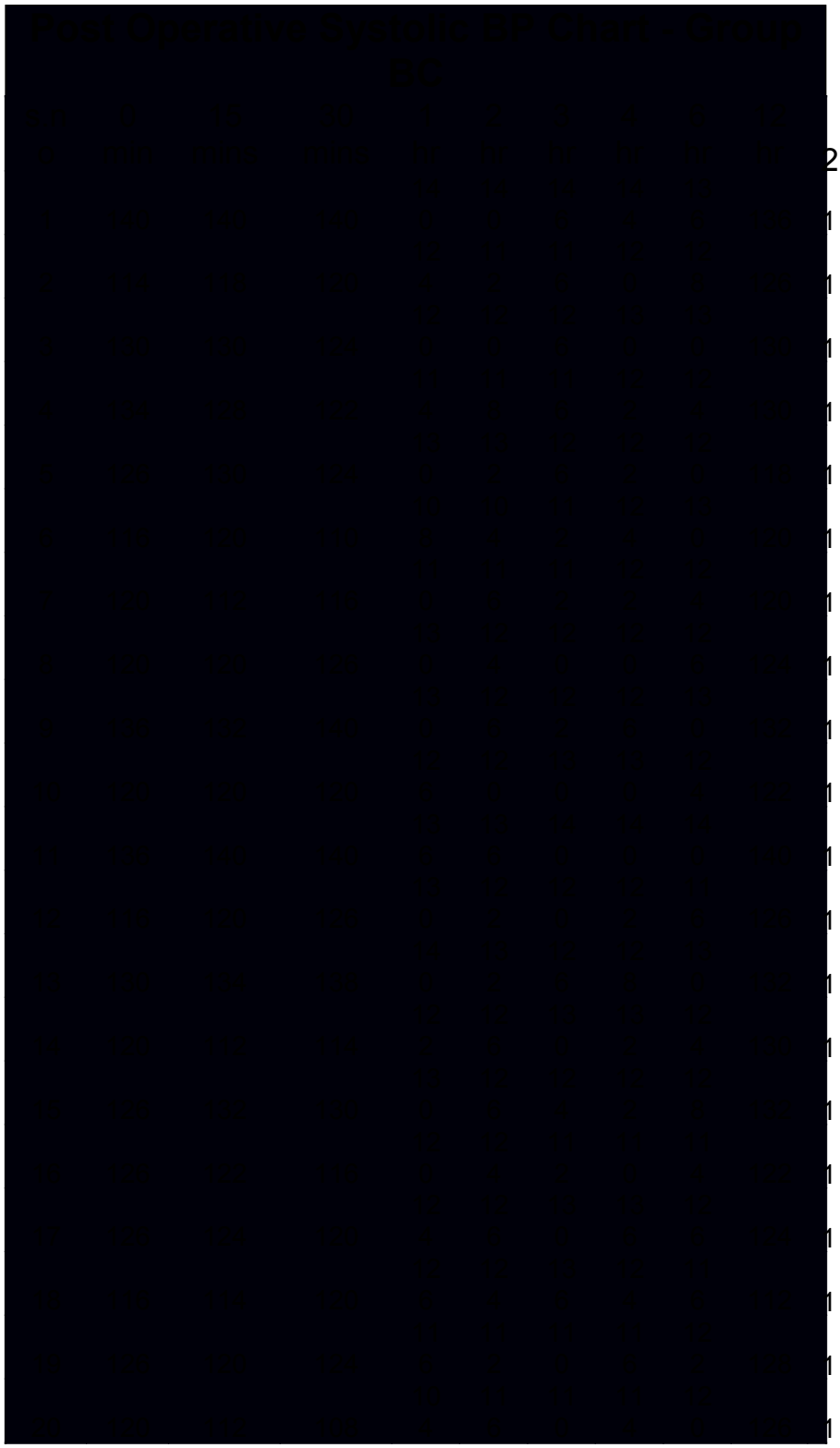



Intra operative diastolic BP Chart - Group BC


Post Operative Pulse Chart - Group BA
S.no
0
min
15
mins
30
mins
1
hr
2
hr
3
hr
4
hr
5
hr
6
hr
12
hr
24
hr

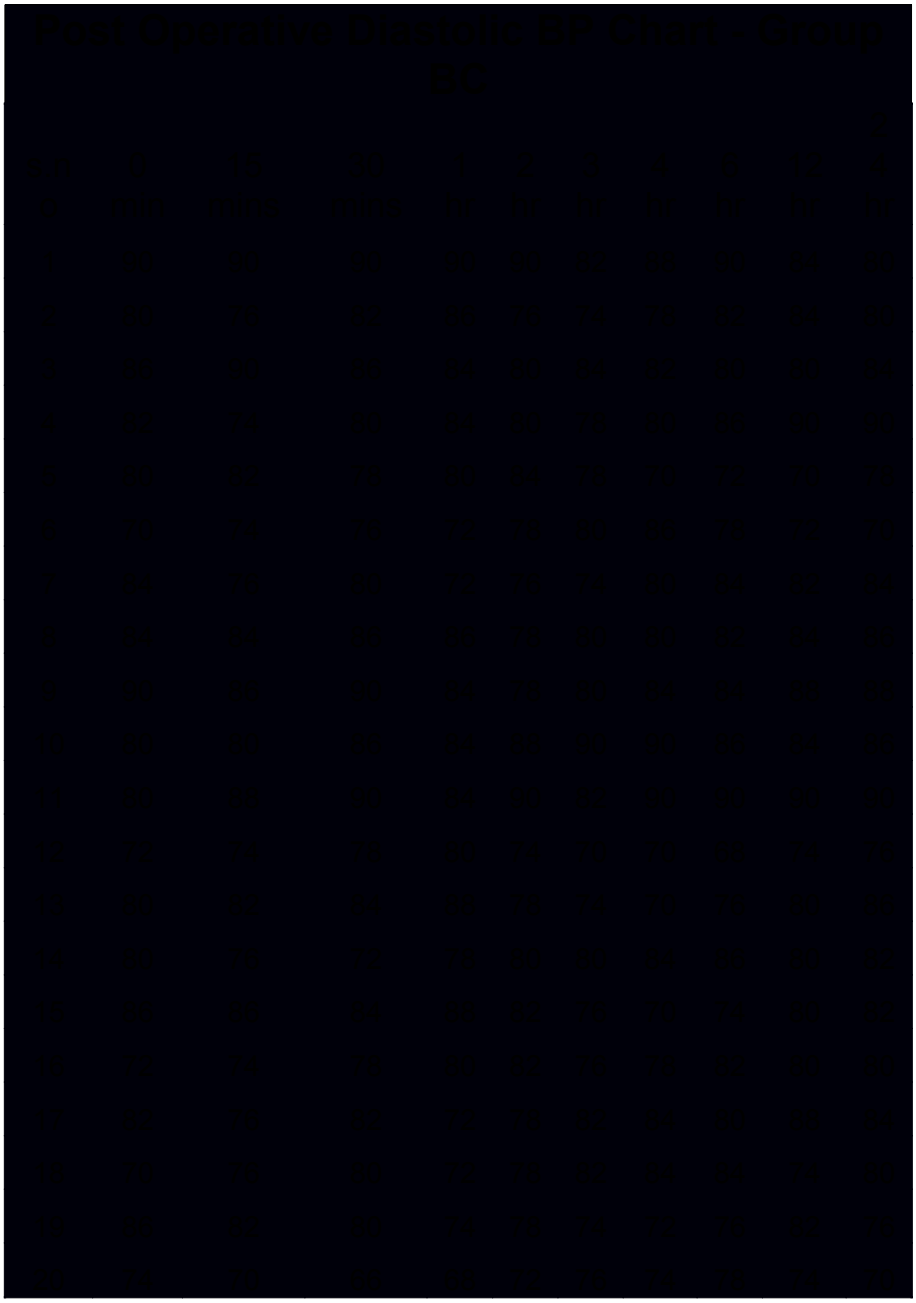

Post Operative Pulse Chart - Group BC

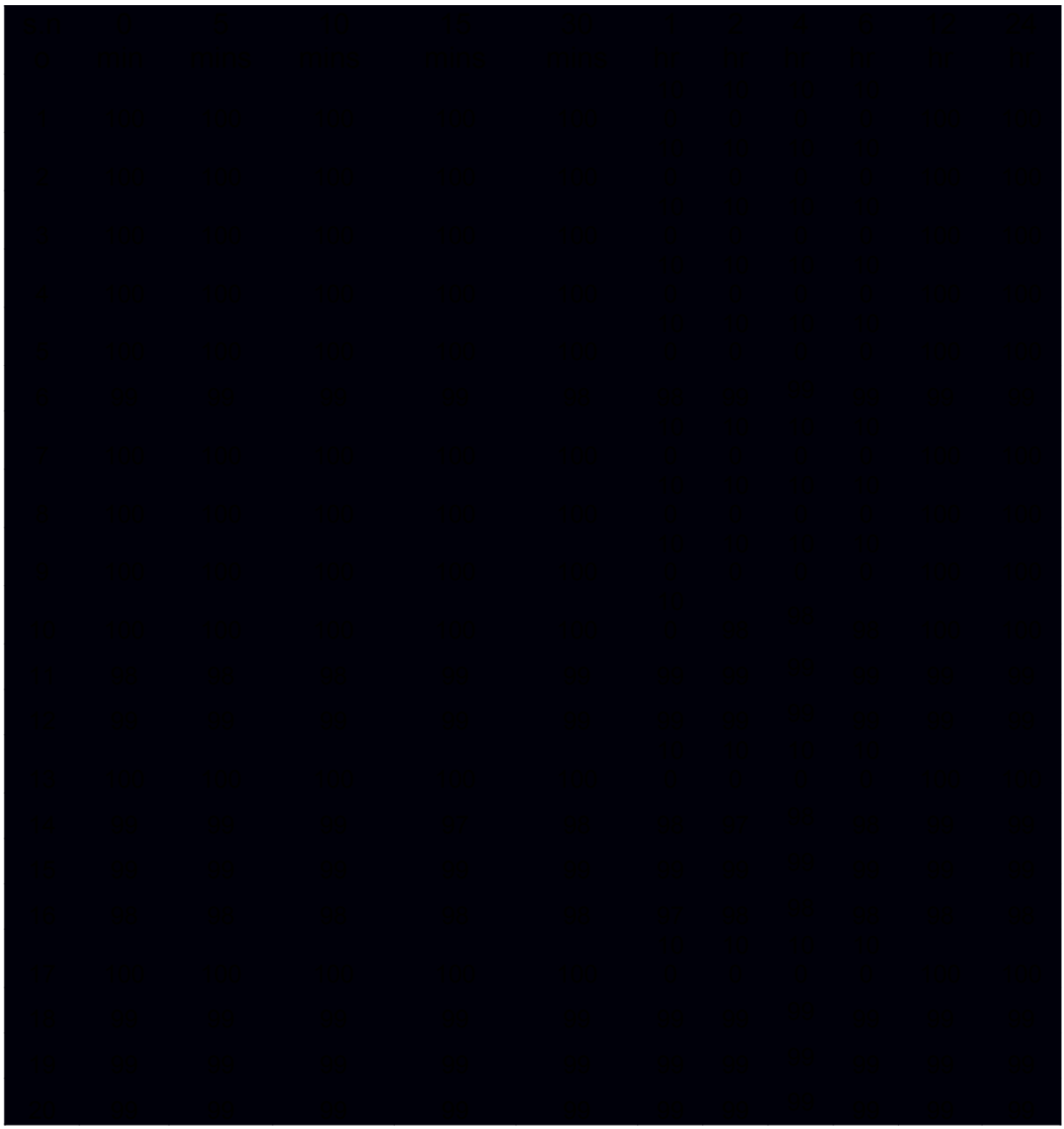

Post Operative Systolic BP Chart - Group 2A


Post Operative Systolic BP Chart - Group 2 &C
Min
0 min
15 mins
30 mins
1 hr
2 hr
3 hr
4 hr
5 hr
6 hr
7 hr
8 hr

Post Operative Diastolic BP Chart - Group 3A

Post Operative Diastolic BP Chart - Group BC






Saturation Chart - Group EC